


# BMJ Open Prescribing patterns for medical treatment of suspected prostatic obstruction: a longitudinal register-based study of the Scottish Health and Social Care Open Data

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## ABSTRACT

**Background** The diagnosis of lower urinary tract symptoms related to suspected bladder outflow obstruction from benign prostate hyperplasia/enlargement in men is increasing. This is leading to high demand on healthcare services; however, there is limited knowledge of differences in pharmacotherapy prescribing for this condition based on geography.

**Objective** To investigate potential variation in drug prescribing for suspected bladder outflow obstruction in Scotland, based on analysis of publicly available data, to identify trends and inform future prescribing.

**Study design** A longitudinal register-based data study of prescribing and patient data publicly available from Scottish registries. All information is available as monthly aggregates at the level of single general practices.

**Setting and participants** 903 (97%) general practices in Scotland, over a 50-month period (October 2015 to November 2019).

**Outcome measurements and statistical analysis** We analysed numbers of daily doses of drugs for suspected bladder outflow obstruction prescribed per month using a Bayesian Poisson regression analysis, incorporating random effects to account for spatial and temporal elements.

**Results** Prescriptions for suspected bladder outflow obstruction medications increased during the observation period (overall average rate of change  $1.24 \pm 0.28$ , ranging from 0.893 in Orkney to 1.95 in Lanarkshire). While some determinants of health inequality regarding prescribing practices across health boards are consistent with those known from the literature, other inequalities remain unexplained after accounting for practice-specific and patient-specific characteristics such as deprivation and rurality.

**Conclusions** Inequalities in prescribing for suspected bladder outflow obstruction medications exist in Scotland, partially ascribable to accepted sociodemographic and geographic factors.

## INTRODUCTION

The incidence of bothersome lower urinary tract symptoms (LUTS) in men, which are

## Strengths and limitations of this study

- This is the first study to investigate spatial and temporal variations in drug-prescribing patterns for bladder outflow obstruction using geostatistical models.
- As such, this data provide a new perspective to inform clinical practice.
- The statistical framework described in this paper is very general and can be readily extended to other settings and conditions.
- Data on drug prescribing in Scotland only exist in the public domain at an aggregate (ie, individual general practitioners' practice or patient list) level, which limits the granularity of the analysis.
- The use of summary data regarding levels of socioeconomic deprivation and rurality of patients reduces the accuracy with which one can estimate the shape of their association with the outcome. These factors are likely to be important in terms of access to healthcare and prescribing.

predominantly attributable to benign prostate hyperplasia (BPH) and/or benign prostatic enlargement causing proven or suspected bladder outflow obstruction (BOO), is increasing globally, resulting in reduced quality of life and increased healthcare expenditure.<sup>1 2</sup> In Scotland, men with suspected or proven BOO are generally managed in primary care with medication prescribed by general practitioners (GPs) and/or specialist practitioners, with such medication either prescribed by GPs alone or as part of shared care with specialists such as urologists.<sup>1</sup> Scottish healthcare services, that treat men with prostate conditions face increased demand resulting from an ageing population, increased prostate cancer (PCa) investigation<sup>3 4</sup> and increased awareness of men's health issues, which is likely to have

impacted on the care of men with bothersome LUTS arising from BOO. Studies reporting the incidence and prevalence of LUTS in men are predominantly cross-sectional in nature, with widely varying results.<sup>5</sup>

Scotland's diverse geography provides an ideal landscape to understand how factors that may impact on prescribing patterns may differ spatially in terms of geography and longitudinally.<sup>6</sup> Prescribing trends in Scotland vary geographically by urban/rural and sociodemographic classifications<sup>6</sup> and by unique regional cultures or as a result of strong 'social patterning', one example being the so-called 'Glasgow effect'.<sup>7,8</sup> Furthermore, it has been acknowledged that aspects regarding individual GP medical practices may contribute to prostate health inequalities across UK.<sup>9,10</sup>

Data regarding the prescription of drugs for the medical management of BOO as a cause for male bothersome LUTS have been used internationally in recent years to increase the understanding of patterns of prescribing within specific populations. This approach can be useful to identify potential demographic inequalities in patient access to healthcare for this condition and to understand the patient experience, predominantly using longitudinal data sets.<sup>11–13</sup> However, to date, there is limited knowledge of how the prescribing patterns for drugs used to treat BOO may differ both spatially and temporally. The increasing availability of high-quality open access healthcare data in Scotland has created the opportunity for a more refined and broader-based analysis of prescribing patterns for BOO.

We investigated the possibility that differences may exist in Scotland in the prescribing patterns of the two main classes of medications used to treat bothersome LUTS secondary to BOO. We performed an analysis of publicly available data in order to identify possible variations in prescribing trends that may help inform future prescribing practice.

## MATERIAL AND METHODS

### Data sources

Data were acquired and linked from numerous independent and publicly accessible sources. The data set comprised information at the level of individual general practices and was created from the following four sources:

1. National Health Service (NHS) Scotland OpenData: drug prescriptions monthly data (<https://www.opendata.nhs.scot/dataset/prescriptions-in-the-community>).
2. Information Services Division Scotland (ISD): practice details, deprivation, rurality (<https://www.isdscotland.org/Health-Topics/General-Practice/>).
3. National Institute for Health and Care Excellence (NICE): daily dosages (<https://www.nice.org.uk>).
4. National Records of Scotland (NRS): postcodes, health boards (<https://www.nrscotland.gov.uk/statistics-and-data/geography/our-products/scottish-postcode-directory/2018-2>).

**Table 1** Variables extracted from the four data sources and used as covariates in the statistical model

Variable	Type	Short description
Drug group	Categorical	$\alpha$ -1 blocker or 5- $\alpha$ reductase inhibitor
GP patient list size	Numerical, time-varying	Number of registered patients per GP practice
GP practice run	Categorical, baseline	Is the practice run by GPs (contract type 17J and 17C), rather than by the NHS (contract type 2C)? Yes/No
Dispensing GP practice	Categorical, baseline	Does the GP practice have a license to dispense medicines? Yes/no
Men 45+	Numerical, time-varying	Proportion of patients that are men aged $\geq 45$ years
Deprived 15	Numerical, time-varying	Proportion of patients under the 15th national percentile of deprivation (SIMD)
Remote	Categorical, time-varying	Modal rurality index among the patients (Scottish Government 8-fold Urban Rural Classification) recoded as remote (4, 5, 7, 8) or non-remote (1, 2, 3, 6). Yes/no
Postcode	Categorical, baseline	GP practice postcode as of 2019
Health board	Categorical, baseline	Name of Scottish Health Board where the GP practice is situated.

GP, general practitioner; NHS, National Health Service; SIMD, Scottish Index of Multiple Deprivation.

The keys used to link the sources were the unique GP practice code and date. The ISD and NRS portals provided information regarding both the medical practice and their patient population. Table 1 contains a list of variables extracted from these sources. We used both deprivation and rurality to account for sociodemographic status. In particular, we used the 2016 Scottish Index of Multiple Deprivation<sup>14</sup> and a recoded version of the 2018 Scottish Government Urban Rural Classification.<sup>15</sup> In addition, the ISD and NRS sources provided GP practice-level information regarding the size of the individual practice patient list, the gender and age distribution and the location of the practice (based on postcode and name of relevant Health Board). All GP practices open for the whole study period (October 2015 to November 2019) were included in the data set (903 of 944, 95.7%, practices in Scotland open as of 1 January 2019). The Scottish Open Data portal provided the prescribed amounts of the drugs of interest per month.

### BOO medications analysed

We specifically focused on the prescribing of  $\alpha$ -1 blocking drugs and 5- $\alpha$  reductase inhibitors as these are the only

**Table 2** Suggested daily dosages of the study  $\alpha$ -1 blockers and 5- $\alpha$  reductase inhibitors according to NICE guidelines

Drug	Drug group	Suggested daily dosage (NICE)
Alfuzosin	$\alpha$ -1 blocker	2.5 mg three times a day 10 mg once daily
Tamsulosin cap/tab	$\alpha$ -1 blocker	400 mcg once daily
Dutasteride	5- $\alpha$ reductase inhibitor	500 mcg once daily
Finasteride	5- $\alpha$ reductase inhibitor	5 mg once daily

NICE, National Institute for Health and Care Excellence.

specific medications used for BOO.  $\alpha$ -1 blockers are the firstline and most commonly used drugs prescribed for LUTS secondary to BOO,<sup>1 16</sup> while 5- $\alpha$  reductase inhibitors are generally recommended where men are considered at high risk of BPH progression due to a significantly enlarged prostate, either as monotherapy or in combination with  $\alpha$ -1 blockers.<sup>1 16 17</sup> The  $\alpha$ -1 blockers alfuzosin and tamsulosin hydrochloride were included in the study; however, doxazosin and terazosin were not included as the amounts of these drugs prescribed were negligible, while doxazosin may be prescribed for hypertension. The 5- $\alpha$  reductase inhibitors, dutasteride and finasteride, were both included in this study. When combined with the suggested daily dosages from the NICE website (see table 2), a proxy for the number of daily doses was constructed by rounding to the nearest integer the following expression:

$$n_{dji} = \frac{\text{\#tablets of drug } d \text{ prescribed during month } t \text{ at practice } i}{\text{daily suggested dosage for drug } j} \quad (1)$$

where  $i$ ,  $d$ , and  $t$  represent the GP practice, drug and month, respectively. In our data set, we have observations for  $i=1, \dots, 903$  GP practices over  $t=1, \dots, 50$  months;  $d$  indexes the drugs reported in table 2. The number of daily doses for each of the drug groups was then constructed by summation of the respective drugs' monthly amounts of daily doses. We denote with  $n_{jti}$  the number of daily doses of drugs belonging to group  $j \in \{\alpha 1 - \text{blocker}, 5 - \alpha \text{ reductase inhibitor}\}$ , prescribed during month  $t$ , at each GP practice  $i$ .

We then used a Poisson model in order to describe the average number of daily doses of BOO medication prescribed each month, accounting for each of the covariates presented in table 1, with additional spatial and temporal random effects. Possible interactions between individual GP practices' prescribing patterns, or geographical location, with the prescribed drug type were also investigated.

Equation 1 describes the model's functional form, while table 3 summarises our choices in terms of spatial and temporal structure. Further details of the statistical analysis are provided as supplementary material.

**Table 3** Spatial and temporal random effects

Parameter	Type	Short description
$\alpha_{[i]}$	Spatial	Intrinsic conditional auto-regressive
$\alpha_{[ij]}$	Unstructured	Unstructured interaction between GP practice and drug type
$\alpha_{[tji]}$	Temporal	First-order auto-regressive, grouped by health board and drug type

GP, general practitioner.

$$\log(\lambda_{jti}) = \alpha + \alpha_{[i]} + \alpha_{[ji]} + \alpha_{[tji]} + \beta_1 \log(\text{list size}_{ii}) + \beta_2 \text{drug group} + \beta_3 \text{contract}_i + \beta_4 \text{dispensing}_i + \beta_5 \text{males } 45p_{ii} + \beta_6 \text{deprived } 15_{ii} + \beta_7 \text{remote}_{ii} \quad (2)$$

where  $j$  (drug group),  $t$  (month) and  $i$  (each GP practice) are as described, and  $\alpha_{[i]}, \alpha_{[ji]}, \alpha_{[tji]}$  denote the random effects, summarised in table 3. A detailed discussion of the choice of the random components of the model is available in online supplemental file 1).

### Computational analysis

All computational analyses were carried out in R 3.6.1.<sup>18</sup> We estimated the model parameters within the Integrated Nested Laplace Approximation framework using the *inla* package.<sup>19</sup> The code is available as online supplemental file 2, while data and shapefiles are from an external repository.<sup>20</sup>

### RESULTS

We investigated the effects of each of the available covariates (including GP practice patient list size; BOO drug group; whether the practice was GP run; whether the GP practice dispensed medication; proportion of men aged 45 years; higher proportion of socioeconomic deprivation and remote/rural location) on the study outcome. Table 4 contains summary statistics on the sample.

Table 5 summarises the output of the Poisson regression estimates of each of the associated parameters. In a further analysis, we interpreted each of these parameters in terms of relative differences from the model average (with the exception of GP practice list size).

The GP practice patient list size was observed to have an effect consistent with an estimated increase of slightly less than one daily dose per month per additional patient (point estimate 0.915). As expected, the prescribed doses of the 5- $\alpha$  reductase inhibitor drug group were observed to be on average less than the prescribed doses of the  $\alpha$ -1 blocker drug group. The estimated relative difference was calculated to be on average 45%–48% fewer 5- $\alpha$  reductase inhibitor drug prescriptions than  $\alpha$ -1 blocker drug prescriptions per month (point estimate 46%).

**Table 4** Summary statistics of the sample, stratified by health board

Health board	Number of practices	Daily doses prescribed/month		Patients list size	Run by GP	Dispensing practices	Men 45+	Highly deprived	Remote practices
		$\alpha$ -1b	5-ari						
Ayrshire and Arran	53	3091 (2563)	1320 (1192)	6625 (4831)	1.00	0.06	0.25 (0.03)	0.20 (0.24)	0.18
Borders	23	2054 (1838)	1374 (983)	4862 (3343)	1.00	0.17	0.26 (0.01)	0.00 (0.09)	0.13
Dumfries and G.	31	2231 (1449)	966 (782)	3976 (3492)	1.00	0.39	0.27 (0.04)	0.00 (0.08)	0.20
Fife	53	2699 (1805)	1372 (820)	6367 (4313)	0.96	0.02	0.23 (0.03)	0.13 (0.23)	0.04
Forth Valley	51	2144 (1767)	1515 (1260)	5844 (4606)	0.94	0.02	0.23 (0.02)	0.06 (0.16)	0.13
G.Glasgow and Clyde	230	1658 (1692)	826 (924)	4863 (3620)	1.00	0.01	0.21 (0.04)	0.33 (0.43)	0.04
Grampian	70	3204 (2595)	1462 (1228)	7980 (4875)	0.94	0.17	0.24 (0.04)	0.00 (0.02)	0.28
Highland	95	1002 (1486)	504 (810)	2358 (4467)	0.85	0.39	0.27 (0.05)	0.00 (0.05)	0.56
Lanarkshire	97	1665 (2161)	1428 (1406)	6048 (4570)	0.99	0.02	0.22 (0.02)	0.23 (0.22)	0.10
Lothian	112	2205 (1700)	1176 (1008)	7814 (4229)	0.95	0.00	0.21 (0.04)	0.02 (0.12)	0.03
Orkney	6	1675 (1217)	1008 (929)	2908 (2379)	0.83	0.33	0.28 (0.03)	0.00 (-)	0.70
Shetland	10	690 (1107)	253 (560)	1143 (1913)	0.20	0.70	0.24 (0.04)	0.00 (-)	0.92
Tayside	63	3103 (2140)	1645 (1166)	6685 (4676)	0.94	0.02	0.23 (0.05)	0.05 (0.24)	0.12
Western I.	9	892 (1891)	588 (665)	1389 (4046)	1.00	0.89	0.30 (0.06)	0.00 (-)	0.76

Number of practices, median and (IQR) for continuous variable, proportions for categorical variables. Counts are rounded to the nearest integer, proportions to the second decimal place.  
GP, general practitioner.

We observed that the nature of how the GP practices are individually run is associated with BOO drug prescribing practice, with GP-run practices (rather than by direct NHS-run practices) having larger volumes of these prescriptions. The model results are consistent with 19%–35% (point estimate 27%) increased number of monthly prescriptions for GP-run practices compared with NHS-run practices, all else being equal. This is an interesting result, and to the best of our knowledge, no rigorous research has been undertaken to investigate the role that how a GP practice is managed plays on

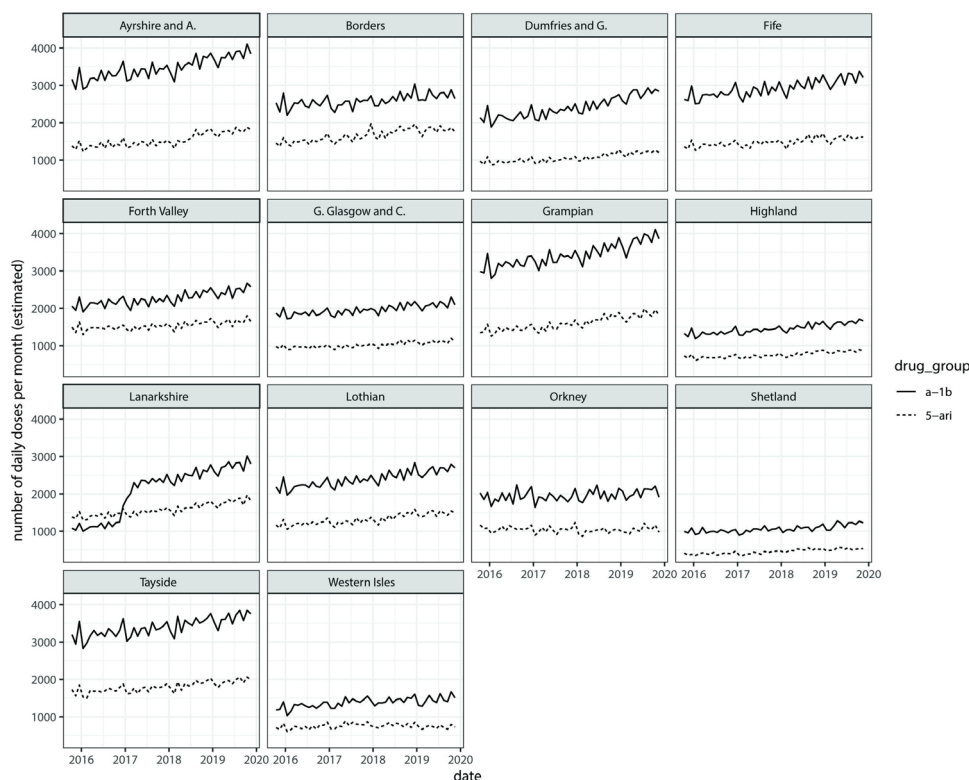
the stability of provision of care and, in turn, on help-seeking behaviours and clinical outcomes. Conversely, we observed that GP-dispensing practices are associated with 3%–13% (point estimate 8%) lower volumes of BOO drug prescriptions compared with GP practices without a pharmacy, keeping all other variables constant. Practices that dispense usually tend to do so because there is no local community pharmacy, and they need one to fit a need; one way of thinking about this is that having a dispensing licence may reflect an aspect of remoteness that is not captured by the rurality measure we employ.

**Table 5** Summary of estimated posterior distributions for the fixed effects, containing the model estimates with associated uncertainty, on the rate ratio scale

	Mean	SD	2.5%	50%	97.5%	Mode
$\alpha$ —Intercept	0.208	0.008	0.192	0.208	0.225	0.208
$\beta_1$ —log(GP practice patient list size)	0.915	0.002	0.911	0.915	0.919	0.915
$\beta_2$ —drug group (5- $\alpha$ reductase inhibitors)	0.536	0.009	0.518	0.535	0.554	0.536
$\beta_3$ —GP run practices	1.269	0.042	1.190	1.268	1.352	1.269
$\beta_4$ —dispensing GP practice	0.918	0.024	0.871	0.917	0.966	0.918
$\beta_5$ —Men aged $\geq 45$ years	1.049	<0.001	1.049	1.049	1.050	1.049
$\beta_6$ —socially deprived area	1.017	0.007	1.003	1.017	1.031	1.017
$\beta_7$ —remote/rural GP practice	1.002	<0.001	1.002	1.002	1.003	1.002

The posterior distribution associated to the patient list size effect estimate  $\beta_1$  was not transformed and should be read on the outcome scale, as explained in-text.  
GP, general practitioner.





**Figure 1** Statistical model average number of daily doses of each BOO drug type prescribed per month, by individual Scottish Health Board and adjusted for GP practice patient roll size. BOO, bladder outflow obstruction; GP, general practitioner.

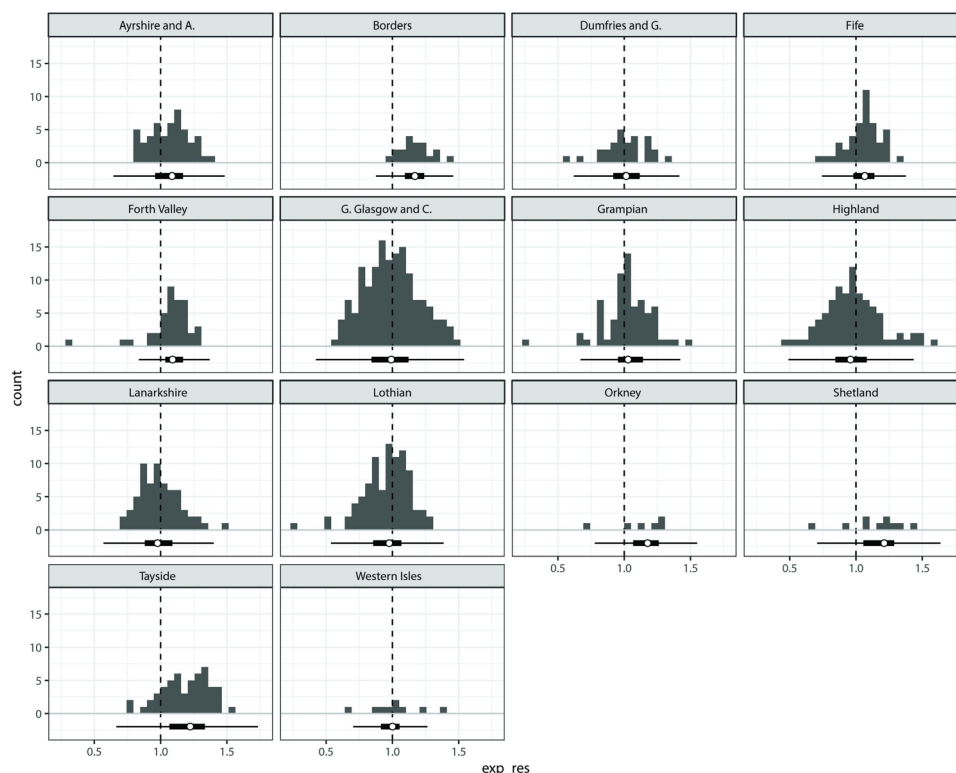
We found the proportion of men aged  $\geq 45$  years in the GP practice patient list to be positively associated with the volume of BOO prescriptions, with an estimated average increase in the monthly rate of prescription of 4.9% per percentage point. In contrast, the levels of deprivation, and a remote/rural geographical location of each GP practice, were found to have a negligible association with prescribing practice.

Next, we investigated the statistical model's interpolations according to Health Board and drug group ( $\alpha$ -1 blocking drugs and 5- $\alpha$  reductase inhibitors) (figure 1). This analysis highlighted a general increase in the volumes of prescriptions for these medications over the 4-year study period. Trends in prescribing were observed to be broadly similar across most Health Boards, with a less prominent increase in less populated areas, which may potentially be attributable to a more stable population structure over the 4-year period of observation as well as unaccounted for differences in help-seeking behaviours. Within most Health Boards, the growth in prescriptions for each drug group was almost parallel during the 4-year observation period, suggesting consistency in terms of increased BOO drug prescribing. Additional observations included a marked shift in volumes of  $\alpha$ -1 blocking drug prescriptions in Lanarkshire between November 2016 and February 2017; however, no further specific information regarding this phenomenon was available within the publicly available data set. In the absence of a reasonable explanation for this singular observation in

this one Health Board, this has been treated as an artefact due to a change in data-recording criteria.

Next, we investigated how the statistical model residuals may provide insight into how BOO drug prescribing behaviour differed across Scotland during the 4-year study period. Figure 2 illustrates histograms of exponentiated residuals for each individual Health Board across Scotland, where a reference value of  $1 = e^0$  represents a null residual (ie, there is no deviation from the model's predicted average). Each residual is specific to one individual anonymous GP practice. On an exponential scale, a value of 1 indicates a prescribing behaviour in line with the average as described by the statistical model across Scotland during the study period. A value below 1 indicates prescribing volumes higher than expected based on the model, while a value larger than 1 indicates prescribing volumes lower than expected. Asymmetry around the reference value of 1, and/or multiple modes of distribution, suggests a different behaviour of individual GP practices within a Health Board compared against the national average across Scotland.

Using this statistical approach, we generally observed consistency in the prescription of drugs for BOO across Health Boards in Scotland, with most distributions appearing to be approximately unimodal and symmetric around the null residual (ie, the reference value of  $1 = e^0$ ). However, some interesting patterns of prescribing can be observed, such as the reduced level of BOO drug prescribing in some individual Health Boards (most



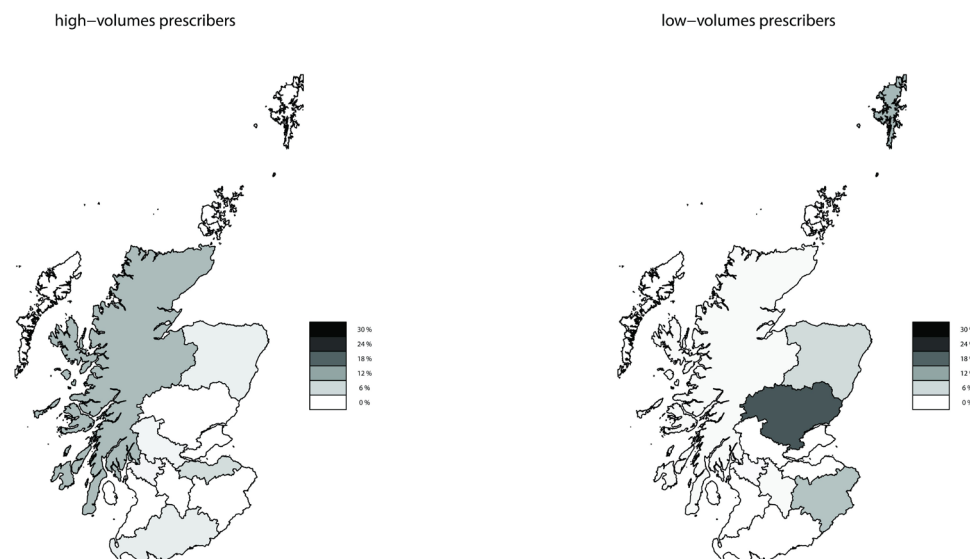
**Figure 2** Frequency histograms of the statistical model's exponentiated residuals for each Scottish Health Board. The vertical dashed line represents the null residual (value=1 on the exponentiated scale), and each small black square represents the average number of daily prescriptions of BOO drugs (combined  $\alpha$ -1 blockers and 5- $\alpha$  reductase inhibitors) per month per individual anonymous GP practice within each Health Board. The boxplot below each histogram illustrates the same data distribution (the white point marks the median, the thick line represents the usual box and the thin line represents the whiskers). Ideally the exponentiated residuals for each GP practice would lie around the null residual (ie, value=1); however, the heterogeneity in prescribing practice is illustrated by increased spread to the left and right of the null residual. A shift of GP practice distributions to the right of the null residual, as seen in Health Boards such as Borders, Fife, Orkney, Shetland and Tayside, illustrates less prescribing of these medications than would be expected. BOO, bladder outflow obstruction; GP, general practitioner.

notably Borders, Forth Valley, Tayside, Orkney and Shetland) compared with the average prescribing rate across Scotland. The reasons for these differences in prescribing pattern in these individual Health Boards are unclear and require further investigation.

Next, we examined the BOO drug-prescribing patterns of GP practices with the aim of assessing and visualising possible spatial patterns. Once again using the model residuals, it was possible to identify individual anonymous practices at the extremes of the BOO prescribing distribution and show their Health Board location on a map. This approach can be useful in order to detect geographic clusters of similar prescribing patterns, while accounting for temporal trends and other potential confounding factors that are already included in the model. For example, the policymaker might be interested in identifying clusters of GP practices where the rates of prescribing are either very low or very high with respect to the national average. We present the results of such analysis in figure 3 where, to preserve anonymity of the individual practices, we have aggregated the information at the Health Board level. We denote those GP practices with a model residual below the 2.5% percentile of the overall distribution of residuals

as 'high-volume prescribers' and those above the 97.5% percentile as 'low-volume prescribers'. We stress that high-volume and low-volume are with respect to the national average as described by the model. Moreover, the quantile thresholds are arbitrary and can be adjusted according to the analytical need.

We observed that Highland is the Health Board with the largest percentage (~9.5%) of GP practices that were identified as being in the upper tail of prescribing volumes (identified by model residuals <2.5% percentile), followed by Lothian (~5.3%), Dumfries and Galloway (~3.2%), Grampian (~2.9%), Forth Valley (~2%) and Greater Glasgow and Clyde (~1.7%). No 'high-volume prescriber' GP practices were found within the remaining Health Boards. On the other hand, Tayside was identified as the Health Board with the largest percentage (~19%) of 'low-volume prescribers' (identified by model residuals >97.5% percentile). Shetland (10%), Borders (~8.7%), Grampian (~5.7%), Highland (~1.1%), Lothian (~1%) and Greater Glasgow and Clyde (~0.9%) also contained GP practices that prescribed far below the national average. The remaining Health Boards did not contain any 'low-volume prescribing' practices. The underlying



**Figure 3** Maps of Scotland highlighting the Health Board locations of anonymous GP practices at the extremes of the distribution of BOO drug prescribing. The left panel shows the percentage of GP practices within each Health Board that have been identified (via model residuals) as being high in prescribing volumes with respect to the national average (ie, model residuals <2.5% percentile). Similarly, the right panel shows the percentage of GP practices low in prescribing volumes with respect to the national average (ie, model residuals >97.5% percentile). BOO, bladder outflow obstruction; GP, general practitioner.

reasons for these observations are currently unclear and require further investigation.

## DISCUSSION

This study has investigated possible differences in patterns of medical prescribing for the two most common classes of drugs (ie,  $\alpha$  – 1 blockers and 5 –  $\alpha$  reductase inhibitors) used to treat BOO in Scotland over a recent 4-year period (October 2015–November 2019) using publicly available data from individual GP practices across all Health Boards. In taking this approach, we have assumed that most BOO medication is prescribed by GPs, either practising alone or on the advice of a specialist prescriber such as a urologist from specialist practice, as is the case throughout the UK. Nevertheless, using this approach and GP practice prescribing data with this assumption, we generated a study data set by linking prescribing data to GP practice-specific information (such as their type of contract with the NHS and their licence to dispense) and summary characteristics of their patient populations (such as patient age and GP practice-associated levels of deprivation and rurality). To our knowledge, this is the first time that particular characteristics of a GP practice have been studied as potential factors influencing BOO drug prescribing patterns in Scotland. This has enabled us to identify trends in prescribing behaviour that may help inform future practice.

A trend of increased BOO drug prescribing practice was observed throughout the 4-year observation window consistent with trends in increased detection of PCa (which is prevalent in men of the same age), an ageing Scottish population, increased awareness of male health

issues among both patients and GPs and increased referral of men to secondary care due to a raised PSA.<sup>21 22</sup>

Though gaining a definite understanding of this trend was outside the scope of this study, in order to fully understand the nature of this increase, it would be pertinent to (1) identify the relative contribution (or otherwise) made by increased referral to secondary care with suspected PCa (as identified by a raised PSA), which might result in increased BOO/BPH prescribing as a secondary consequence of a raised PSA referral, (2) the currently unaccounted for impact of increased GP and public awareness and public help seeking behaviour and (3) increased focus on PCa management, rather than BPH surgery, which may have contributed to the increase in medical drug use for BOO, rather than definitive intervention, though this is speculative. Greater understanding of these issues will facilitate planning to meet demand in primary care services given ongoing capacity shortage, and also secondary care as increased pharmacological treatment could be indicative of future demand for surgery.<sup>23</sup>

Whether practices were NHS or GP-run, or had a dispensing pharmacy present within the GP practice, were associated with higher and lower prescribing volumes, respectively. While the individual characteristics of GP medical practices are known to differ by region<sup>24</sup> research accounting for these factors is relatively sparse; hence, it is unclear why this difference exists. Furthermore, although regional prescribing behaviours were largely uniform, lower levels of prescribing were noted in some individual Health Boards. No clear explanation could be given for this observation, as no possible explanatory factor is common to these Health Boards. An

investigation of factors listed above would be pertinent to understand regional differences evident in prescribing behaviours and guide intervention to reduce inequity.

This study found several GP practices operating at the extremes of prescribing, with practices across five Health Boards prescribing considerably more, and practices across seven Health Boards prescribing considerably less, of each drug than other Scottish practices. In particular, 19% of GP practices in Tayside were considered to be 'low-volume prescribers', which could partially explain why Tayside was found to have lower overall levels of prescribing. However, there was otherwise no correlation between individual GP practice prescribing behaviours and overall volume of prescriptions within the Health Board. As such, this study found that factors other than GP list size or accepted sociodemographic and geographic measures may be contributing to inequalities in prescribing practice. Further research is needed to identify these factors, although individual GP attitudes and understanding of prostate diseases,<sup>9 10</sup> and Scotland's cultural diversity,<sup>7 8 18</sup> may be potential explanations.

The data used in this research had several limitations. First, the available data only exist in the public domain at an aggregate level (ie, individual GP practice or patient list), and further information would be helpful in order to identify the reasons why prescribing practices vary at a more granular level (perhaps by associating the prescribing practice with the presence or absence of a GP with a particular interest in men's health issues, as an example). Second, the use of summary data regarding levels of socioeconomic deprivation and rurality of patients reduces the accuracy with which one can estimate the shape of their association with the outcome, with these factors likely to be important in terms of access to healthcare and prescribing. Third, not having information about specific GP practice catchment areas made it necessary to use an adjacency matrix based on postcodes, rather than actual distances, resulting in a suboptimal method of accounting for underlying spatial processes. Fourth, we have not investigated how differences in GP prescribing practices for BOO may impact on the rates of surgical management of this condition. For example, a study in Australia identified regional differences in the surgical management of BOO secondary to BPH<sup>23</sup>; it would be interesting for future research to potentially link BPH prescribing practice with rates of surgical management of this condition. For example, it might be the case that medical therapy can delay the need for surgery by a number of years, or reduced rates of BPH prescribing in any particular Health Board may be associated with higher rates of surgical intervention. These hypotheses require testing in data sets if they can be linked.

Further research to identify factors that lead to inequality in primary care practice is needed, and these is a need for data collection and data sharing to develop to enable this. It would also be interesting for future research to investigate trends and potential inequalities regarding all prostate-related conditions (both benign

and malignant) over space and time in other settings and geographical locations. In particular, it would be interesting to investigate whether the trends observed in Scotland may similarly exist in other regions of the UK, and if so, are variations attributable to common factors such as urban/rural and socioeconomic status. In addition, the general nature of the statistical modelling framework we have proposed in this study may be extended to investigate other kinds of models, covariates and medical conditions in a range of future studies.

## CONCLUSIONS

The volume of prescriptions of drugs for LUTS secondary to BOO has steadily increased across Scotland during a recent 4-year observation period, consistent with trends in PCa, which similarly affects men of this age. Regional differences in the volume of prescribed drugs, and extremes in individual GP practice prescribing patterns, were found. While prescribing patterns varied in relation to geographic and demographic factors and GP practice list size, this study identified considerable variations that could not easily be accounted for. Potential explanations for these variations include individual GP attitudes and understanding of prostate diseases<sup>9 10</sup> and Scotland's cultural diversity.<sup>6-8</sup>

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**Contributors** FA and AW initiated the study. FA and EG developed the statistical model. FA had full access to all the data in the study, carried out the statistical analysis and took responsibility its accuracy and for the integrity of the data. FA drafted the manuscript, and all authors (FA, RB, EG, AEW, AW) contributed to the critical revision for important intellectual content, and to the interpretation of the data analysis results. RB and AEW provided advice on clinical aspects of the results.

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**Technical supplement for the paper “Prescribing patterns for medical treatment of suspected prostatic obstruction: a longitudinal register-based study the Scottish Health and Social Care Open Data”**

Authors: Federico Andreis, Richard Bryant, Emanuele Giorgi, Andrea Williamson, Ashleigh Ward

We employ a Bayesian hierarchical Poisson model that estimates spatial and temporal structured patterns. The outcome of interest is the number of daily doses prescribed in a month at a general practice in Scotland, between October 2015 and November 2019. Let  $n_{jti}$  denote the number of prescriptions of drugs belonging to group  $j \in \{\alpha - 1b, 5 - \alpha ri\}$ , for practice  $i = 1, \dots, 903$ , in month  $t = 1, \dots, 50$ .

Conditionally on a set of random effects  $\alpha_{[i]}$ ,  $\alpha_{[ji]}$  and  $\alpha_{[t]}$ , let  $n_{jti}$  follow a Poisson distribution with parameter  $\lambda_{jti}$ , modelled with an additive linear predictor on a natural logarithm scale:

$$n_{jti} \sim \text{Poisson}(\lambda_{jti})$$

$$\log(\lambda_{jti}) = \alpha + \alpha_{[i]} + \alpha_{[ji]} + \alpha_{[tji]} + \beta_1 \log(\text{list size}_{ti}) + \beta_2 \text{drug group} + \beta_3 \text{contract}_i + \beta_4 \text{dispensing}_i + \beta_5 \text{males 45p}_{ti} + \beta_6 \text{deprived 15}_{ti} + \beta_7 \text{remote}_{ti}$$

The random effects, as described in Table 3 in the paper, relate to:

- A structured component accounting for spatial correlation ( $\alpha_{[i]}$ )
- An unstructured component accounting for potential interactions between individual practice and type of drug ( $\alpha_{[ji]}$ )
- A component accounting for temporal correlation, grouped by health board and type of drug ( $\alpha_{[t]}$ ).

23 To model the spatial component  $\alpha_{[i]}$ , we employ an intrinsic Conditional Auto  
24 Regressive (iCAR [1,2,3]) structure that exploits an adjacency matrix based on  
25 location of the practices. The postcodes are linked to Easting/Northing coordinates  
26 and Voronoi tessellation is used to find nearest neighbours and their distances (this  
27 was done using the *caramellar* package, available from github via  
28 `devtools::install_github("barryrowlingson/caramellar")`). In this way, the model allows  
29 the borrowing of strength of information across neighbouring regions.

30 The component accounting for potential interactions between the individual medical  
31 practice and the type of drug prescribed  $\alpha_{[ji]}$  is modelled in an unstructured way,  
32 using *iid* gaussian terms with common precision parameter [3].

33 The temporal component  $\alpha_{[t]}$  is modelled using a first-order autoregressive process  
34 [1], allowing grouping by health board and drug type. This approach allows the  
35 estimation of a common temporal autocorrelation structure for practices in the same  
36 health board and with respect to the same drug group type.

37 An Integrated Nested Laplace Approximation [4] approach is used to approximate  
38 the posterior distribution and obtain the estimates, using the *inla* package in R;  
39 default prior distributions are used for all parameters. To make estimation  
40 computationally easier, a cheap Gaussian approximation is first used and the  
41 resulting estimates employed as reasonable starting values for the actual model  
42 fitting procedure (details in the R code in Supplement 2). Kullback-Leibler divergence  
43 statistics [3] indicate a satisfactory approximation to all marginal posterior densities.

44 Figure 1 contains the summary of the model fit, while Table 1 contains a summary of  
45 estimated posterior distributions for the random effects in terms of standard  
46 deviations, rather than precision parameters (as in Figure 1). Estimation took

47 approximately 7 hours on an AMD Ryzen 7 2700x processor with 32GB DDR4 RAM,  
 48 under Windows 10.

49 Figure 1. Summary of model fit

```
call:
  c("inla(formula = formula_mod_IV, family = \"poisson\", data = df_joint, \"\", \" verbose = TRUE,
    control.compute = control$compute, control.predictor = control$predictor, \"\", \" control.inla =
    list(diagonal = 10), control.results = control$results, \"\", \" control.fixed = list(prec.intercept =
    0.1), control.mode = list(result = mod_inla_approx_IV, \"\", \" restart = TRUE))")
Time used:
  Pre = 0.612, Running = 24085, Post = 4.97, Total = 24091
Fixed effects:
      mean      sd 0.025quant 0.5quant 0.975quant      mode kld
(Intercept)  -1.570 0.040    -1.648   -1.570    -1.492 -1.570  0
drug_group5-ari -0.625 0.017    -0.658   -0.625    -0.591 -0.625  0
gp_runY       0.238 0.033     0.174    0.238     0.302 0.238  0
dispensingY   -0.086 0.026    -0.138   -0.086    -0.035 -0.086  0
log(list_size) 0.915 0.002     0.911    0.915     0.919 0.915  0
prop_m_45p    4.816 0.032     4.754    4.816     4.879 4.816  0
p_15          0.017 0.007     0.003    0.017     0.030 0.017  0
ur_codeRemote  0.002 0.000     0.002    0.002     0.003 0.002  0

Random effects:
  Name      Model
  postcode_n Besags ICAR model
  time_n     ARI model
  gp_drug    IID model

Model hyperparameters:
      mean      sd 0.025quant 0.5quant 0.975quant      mode
Precision for postcode_n 4.353 0.328     3.753    4.337     5.039 4.302
Precision for time_n    29.235 5.693    18.647    29.144    40.766 29.217
Rho for time_n         0.899 0.013     0.871    0.900     0.923 0.901
GroupRho for time_n    0.685 0.043     0.604    0.683     0.771 0.676
Precision for gp_drug   20.286 0.802    18.736    20.277    21.895 20.269

Expected number of effective parameters(stddev): 4095.95(1.50)
Number of equivalent replicates : 22.01

Deviance Information Criterion (DIC) .....: 4371157.00
Deviance Information Criterion (DIC, saturated) .....: 3605454.27
Effective number of parameters .....: 4097.92

Watanabe-Akaike information criterion (WAIC) ...: 4488316.21
Effective number of parameters .....: 159926.14

Marginal log-Likelihood: -2217597.61
CPO and PIT are computed

Posterior marginals for the linear predictor and
the fitted values are computed
```

51 Table 1. Summary of estimated posterior distributions for random effects. SD denotes the standard  
 52 deviation.

	mean	Sd	2.5%	50%	97.5%	mode
SD of $\alpha_{[i]}$ (spatial)	0.480	0.018	0.446	0.480	0.516	0.480
SD of $\alpha_{[ji]}$ (unstructured)	0.222	0.004	0.214	0.222	0.231	0.222
SD of $\alpha_{[tji]}$ (temporal)	0.188	0.019	0.157	0.185	0.231	0.178
$\rho_1$ of $\alpha_{[tji]}$ (autocorrelation)	0.899	0.013	0.871	0.900	0.923	0.901
$\rho_2$ of $\alpha_{[tji]}$ (group correlation)	0.685	0.043	0.604	0.683	0.771	0.676



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```
#####  
# Code to reproduce the analyses and the plots in the the manuscript #  
# "Prescribing patterns for medical treatment of suspected prostatic #  
# obstruction: a longitudinal register-based study the Scottish #  
# Health and Social Care Open Data" (2020) #  
# Authors: Federico Andreis, Richard Bryant, Emanuele Giorgi, #  
# Andrea Williamson, Ashleigh Ward #  
#####  
  
#####  
# Code by: Federico Andreis #  
#####  
  
#####  
# libraries #  
#####  
library(tidyverse) # to manipulate data objects  
  
library(rgdal) # to deal with spatial objects  
library(sf)  
library(raster)  
  
library(caramellar) # to build the adjacency matrix, not on CRAN  
#  
devtools::install_github("barryrowlingson/caramellar")  
  
library(INLA) # to fit the model  
library(brinla) # to manipulate inla objects  
  
#####  
# load the dataset and the shapefile #  
#####  
dataset <- read_csv('dataset.csv')  
  
map_scotland_hb <- readOGR('SG_NHS_HealthBoards_2018.shp')  
  
#####  
# create adjacency matrix #  
#####  
  
# create adjacency matrix and transform it into an inla graph  
adjacency_graph <- voronoi_adjacency(dataset %>%  
  group_by(postcode_n) %>%  
  slice(1) %>%  
  
dplyr::select(postcode_n, Easting, Northing) %>%  
  ungroup,  
  
postcode_n~Easting+Northing)$Adjacencies %>% inla.read.graph  
  
#####  
# fit the model #  
#####  
  
# set inla controls  
control <-list(predictor=list(compute=TRUE, link=1),  
  results=list(return.marginals.random=TRUE,  
    return.marginals.predictor=TRUE),
```

```

compute=list(hyperpar=TRUE, return.marginals=TRUE,
             dic=TRUE, mlik=TRUE, cpo=TRUE, po=TRUE,
             waic=TRUE, graph=TRUE, gdensity=TRUE))

# model specification
model <- n_daily_doses~drug_group+gp_run+dispensing+      # fixed effects
              log(list_size)+prop_m_45p+p_15+ur_code+    # fixed effects
  f(postcode_n,model='besag',graph=adjacency_graph)+      # structured
spatial component (iCAR)
  f(time_n,model='ar1',group=hb_drug)+                    # temporal
component (grouped AR1)
  f(gp_drug,model='iid')                                  # unstructured
spatial component (iid)

# fit the model using a cheap Gaussian approximation to obtain reasonable
starting values
# run time ~18 minutes on a AMD Ryzen 7 2700x processor with 32GB DDR4
RAM, under Windows 10
cheap_approximation <- inla(model,
                           family='poisson',
                           data=dataset,
                           control.inla=list(diagonal=100,
                                              strategy="gaussian",
                                              int.strategy="eb"),
                           control.compute=control$compute,
                           control.predictor=control$predictor,
                           control.results=control$results,
                           verbose=TRUE)

# use the command
#
# model_fit <- cheap_approximation
#
# and ignore the following model fit block to be able to use the rest of
the
# code without having to wait for the more accurate approximation to be
obtained
# Note: if you use this approach, the resulting estimates and plots will
differ
# from those in the paper

# fit the model using the cheap approximation estimates as starting
values
# note: this step takes ~7 hours on the machine described earlier
model_fit <- inla(model,
                  family='poisson',
                  data=dataset,
                  control.inla=list(diagonal=10),
                  control.fixed = list(prec.intercept = 0.1),
                  control.compute=control$compute,
                  control.predictor=control$predictor,
                  control.results=control$results,
                  control.mode=list(result=cheap_approximation,
                                   restart=TRUE),
                  verbose=TRUE)

rm(adjacency_graph,control,

```

```
    model,cheap_approximation) # clean up

#####
# post-processing of the model output #
#####

# add the fitted values to the dataset and make health board names into
factors
dataset <- dataset %>%
  mutate(fitted=model_fit$summary.fitted.values$mean,
         hb_name=factor(hb_name))

# obtain predictions by health board and drug group
average_fitted <- dataset %>%
  group_by(time=time,hb_name,drug_group) %>%
  summarise(avg_fitted=mean(fitted),
            avg_observed=mean(n_daily_doses))

# extract the exponentiated spatial residuals and add them to the dataset
exp_residuals <- numeric(length(model_fit$marginals.random$postcode_n))

for (i in 1:length(exp_residuals)) {

  tmp <- model_fit$marginals.random$postcode_n[[i]]

  exp_residuals[i] <- inla.emarginal(exp,tmp) # exponentiate the spatial
residuals

}

rm(tmp,i) # clean up

# make the residuals into a tibble that also contains the practice
postcodes
# and health boards names
exp_residuals <- data.frame(postcode_n=1:length(exp_residuals),
                           postcode=unique(dataset$postcode),
                           exp_residuals=exp_residuals) %>%
  mutate(postcode=as.character(postcode)) %>%
  left_join(.,dataset %>%
            dplyr::select(postcode,hb_name),
            by=c('postcode','postcode')) %>%
  group_by(postcode) %>%
  slice(1)

# add the exponentiated residuals to the dataset
dataset <- left_join(dataset,
                    exp_residuals %>%
                    dplyr::select(postcode_n,exp_residuals),
                    by='postcode_n')

# set up the shapefile and data needed to to plot the map in Figure 3
geo_df <- dataset
coordinates(geo_df) <- ~Easting+Northing
crop_map_hb <- crop(map_scotland_hb,geo_df)

rm(map_scotland_hb) # clean up
```



```
# obtain the quantiles of the exponentiate residuals distribution
# residuals are constant for each GP practice, extract only one line each
dataset_singletons <- dataset %>%
  group_by(gp_code) %>%
  slice(1) %>%
  ungroup

exp_residuals_quantiles <- quantile(dataset_singletons$exp_residuals,
                                   p=seq(0,1,by=.025))

#####
# produce the plots in the paper #
#####

# Figure 1
average_fitted %>%
  ggplot(aes(x=time))+
  geom_line(aes(y=avg_fitted,linetype=drug_group))+
  theme_bw()+facet_wrap(~hb_name)+
  xlab('date')+ylab('number of daily doses per month (estimated)')

# Figure 2
exp_residuals %>%
  group_by(hb_name) %>%
  mutate(q1=quantile(exp_residuals,.25),
         q2=quantile(exp_residuals,.5),
         q3=quantile(exp_residuals,.75),
         w=1.5*(q3-q1)) %>%
  ungroup %>%
  ggplot()+geom_histogram(aes(exp_residuals))+
  geom_vline(xintercept = 1, lty=2)+
  ylim(-3,18)+
  geom_hline(yintercept=0,col='grey')+
  geom_segment(aes(y=-2,yend=-2,x=q1-w,xend=q1))+
  geom_segment(aes(y=-2,yend=-2,x=q1,xend=q3),lwd=2)+
  geom_segment(aes(y=-2,yend=-2,x=q3,xend=q3+w))+
  geom_point(aes(y=-2,x=q2),lwd=2,pch=16,col='white')+
  geom_point(aes(y=-2,x=q2),lwd=2,pch=1)+
  theme_bw()+facet_wrap(~hb_name)

# Figure 3

# change quantiles as needed
lower_quantile <- 2 # corresponding to 2.5% in the quantiles vector
upper_quantile <- 40 # corresponding to 97.5% in the quantiles vector

# create the proportions of GP practices meeting the quantile
requirements
prop_q_by_hb <- dataset_singletons %>%
  group_by(hb_name) %>%
  summarise(HBCode=first(hb_code),
            prop_l_q2.5=mean(exp_res<quant_res[2]),
            prop_g_q97.5=mean(exp_res>quant_res[40]))

crop_map_hb@data <- crop_map_hb@data %>%
  left_join(prop_q_by_hb,by='HBCode')

# define a scaling factor for the grey scale: the max observed proportion
```

```
# is slightly less than 0.2, rescaling aids visualisation
scale_factor <- .3

par(mfrow=c(1,2))
plot(crop_map_hb,
     main='high-volumes prescribers',
     #border='black',
     col=grey(1-crop_map_hb$prop_l_q2.5/scale_factor))

for (i in 0:5) {

  rect(470000,750000+i*20000,520000,750000+(i+1)*20000,
       col=grey(seq(1,0,length.out=6))[i+1])
  text(x=545000,y=760000+i*20000,
       paste0(round(scale_factor*seq(0,1,length.out=6)[i+1]*100,2),' %'),
       cex=.5)
}

plot(crop_map_hb,
     main='low-volumes prescribers',
     #border='black',
     col=grey(1-crop_map_hb$prop_g_q97.5/scale_factor))

for (i in 0:5) {

  rect(470000,750000+i*20000,520000,750000+(i+1)*20000,
       col=grey(seq(1,0,length.out=6))[i+1])
  text(x=545000,y=760000+i*20000,
       paste0(round(scale_factor*seq(0,1,length.out=6)[i+1]*100,2),' %'),
       cex=.5)
}
par(mfrow=c(1,1))

rm(prop_q_by_hb,scale_factor,
    lower_quantile,upper_quantile) # clean up

#####
# posterior distributions summary #
#####

# table of fixed effects posterior estimates
model_fit$summary.fixed

# table of random effects posterior estimates
model_fit$summary.random # expressed in terms of precision
bri.hyperpar.summary(model_fit) # expressed in terms of standard
deviation
```